Predicting the efficacy of experimental protocols for the measurement of neuronal parameters using computer simulations and statistical inference

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Description of a neuron

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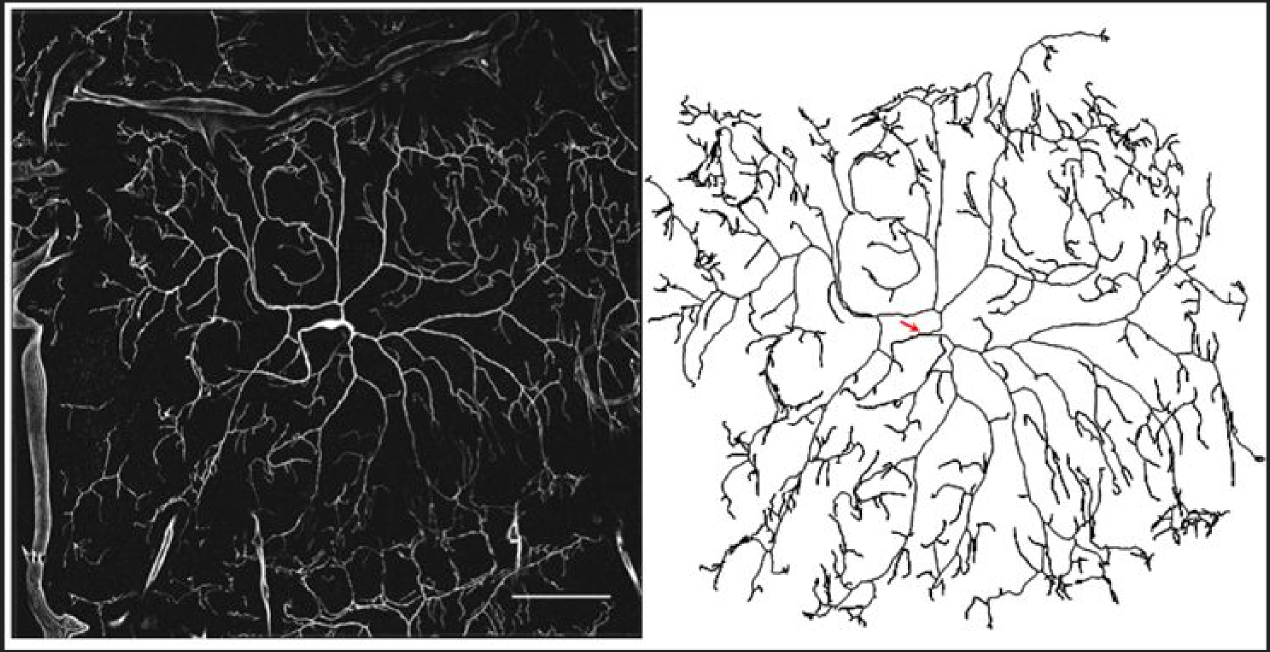

reference: http://howardlab.yale.edu/research/branching-morphology-neurons

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and by its biophysical properties

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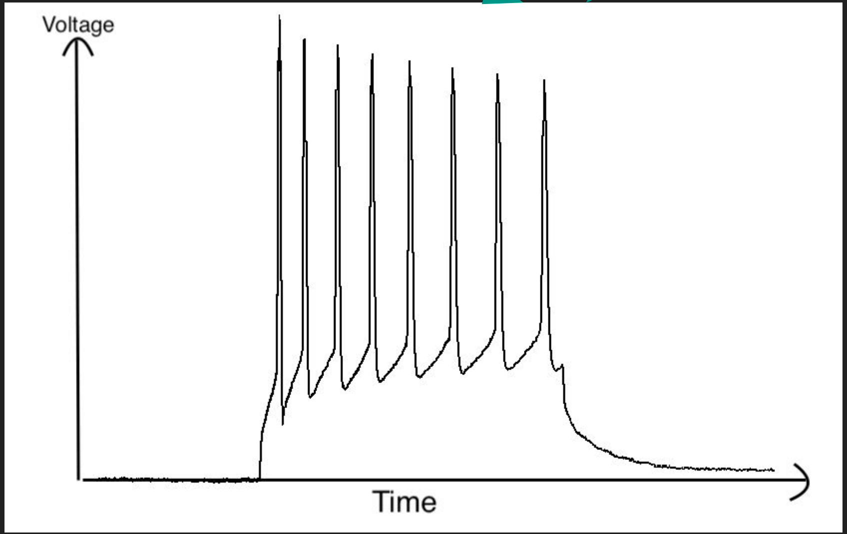
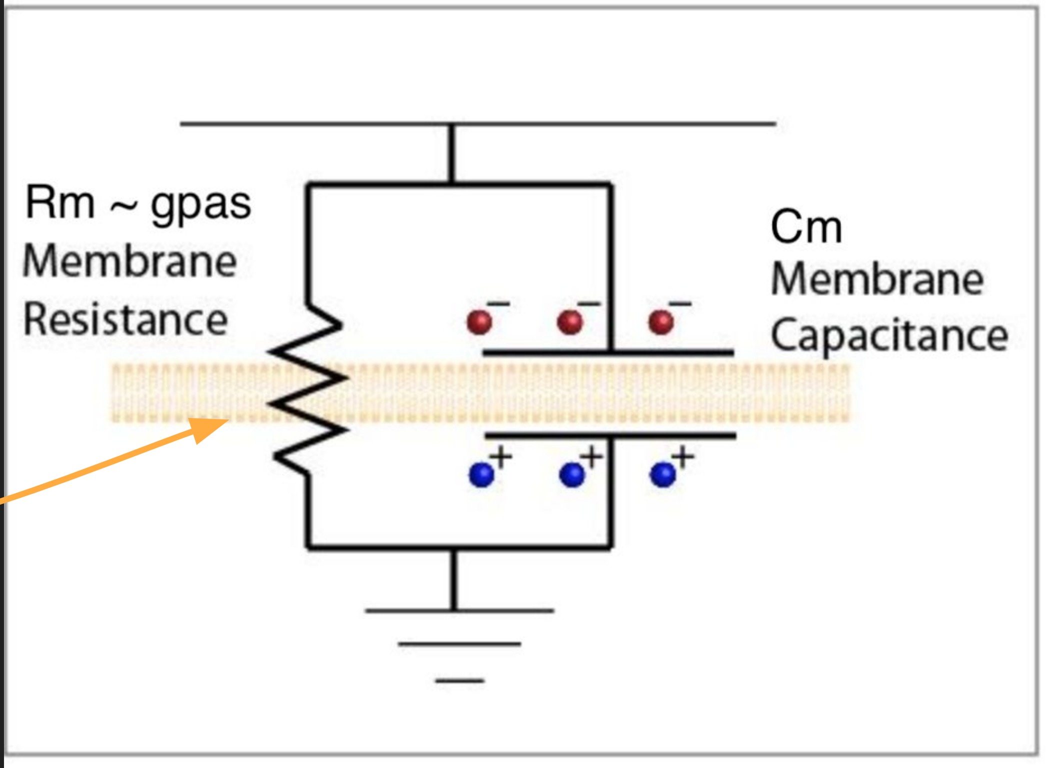


reference: https://upload.wikimedia.org/wikipedia/commons/0/01/Current_Clamp_recording_of_Neuron.GIF

Passive parameters of a neuron

gpas: Leak conductance that is inversely proportional to membrane resistance.



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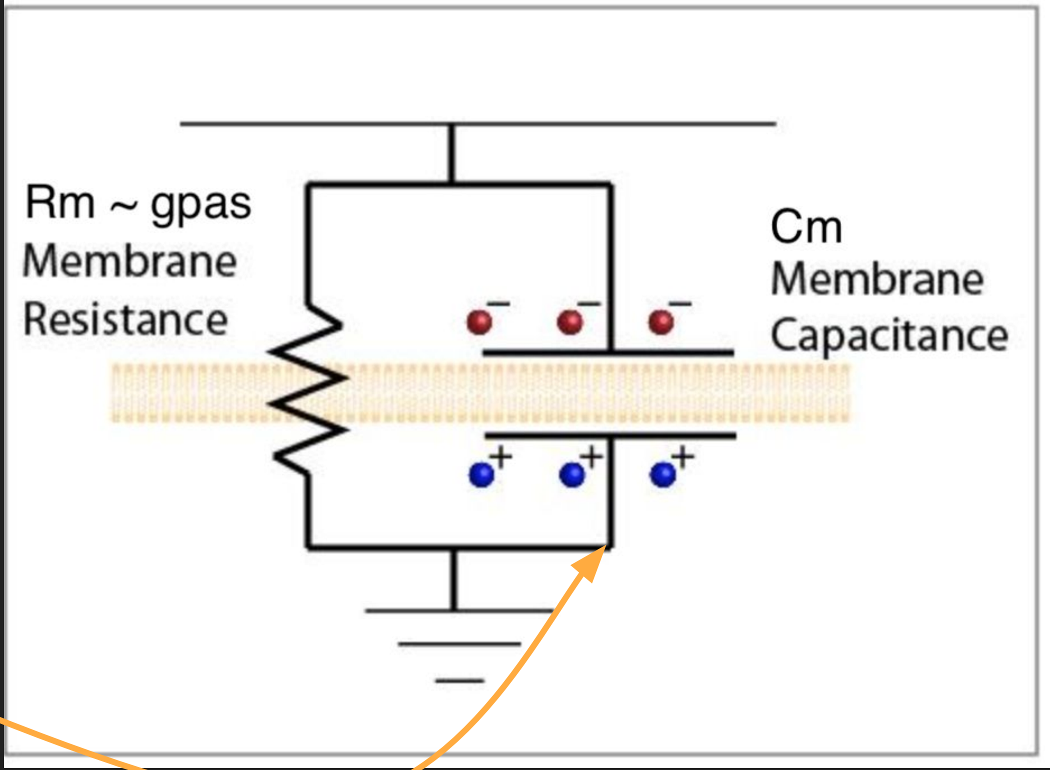
cm: membrane capacitance



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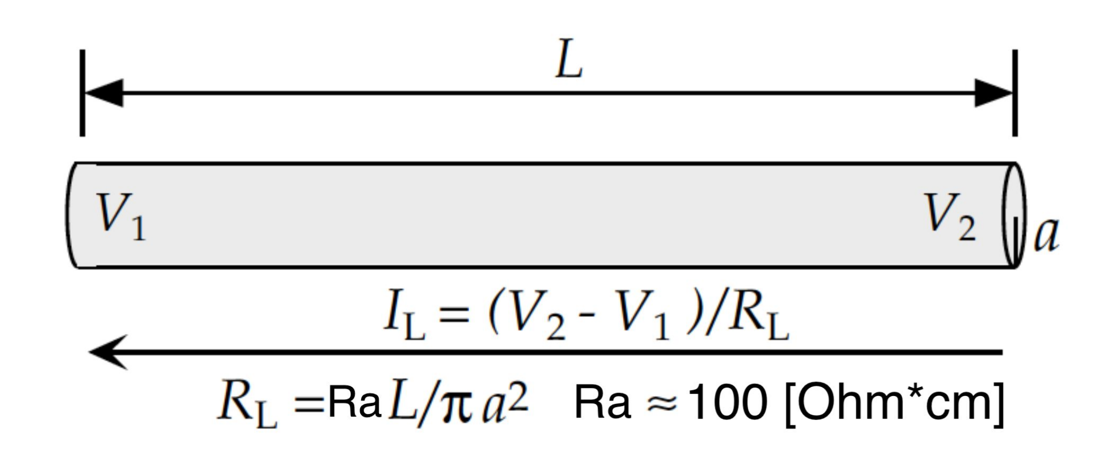
Passive parameters of a neuron

gpas: Leak conductance that is inversely proportional to membrane resistance

cm: membrane capacitance

Ra: axial resistance



reference: https://www.amazon.com/Theoretical-Neuroscience-Computational-Mathematical-Modeling/dp/0262541858

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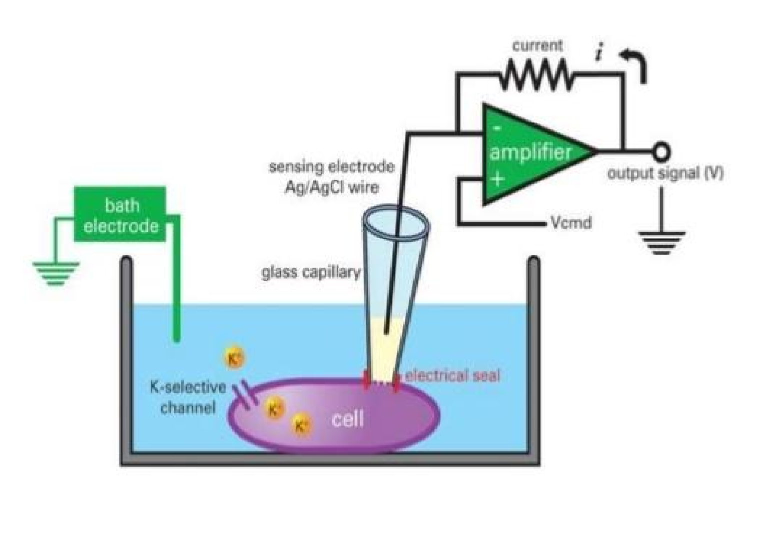

reference:
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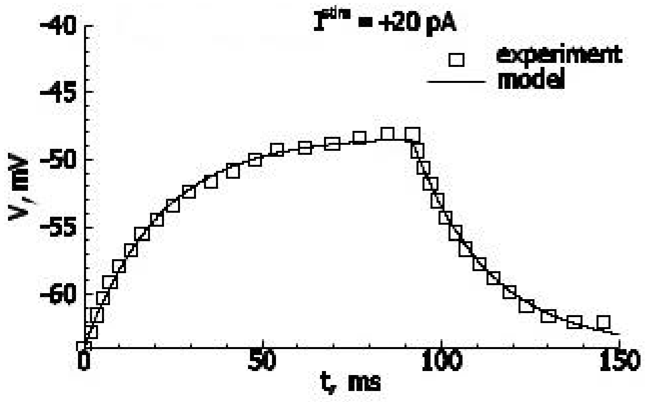
A less invasive and experimentally less complicated method would be beneficial to obtain these parameters

Parameter fitting

Build a mathematical model of the neuron.

$$\tau \frac{dV}{dt} + V = \frac{I}{G}$$



Parameters found by fitting:

$$\tau = 21.4\,ms$$

$$G = 1.27\,nS$$

reference:
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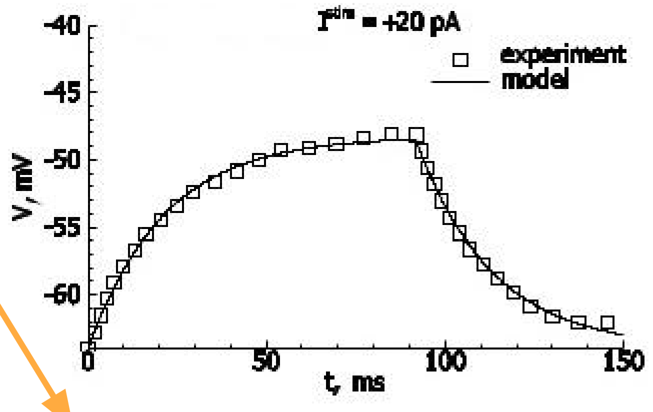
Tune the parameters of the model to fit the data.



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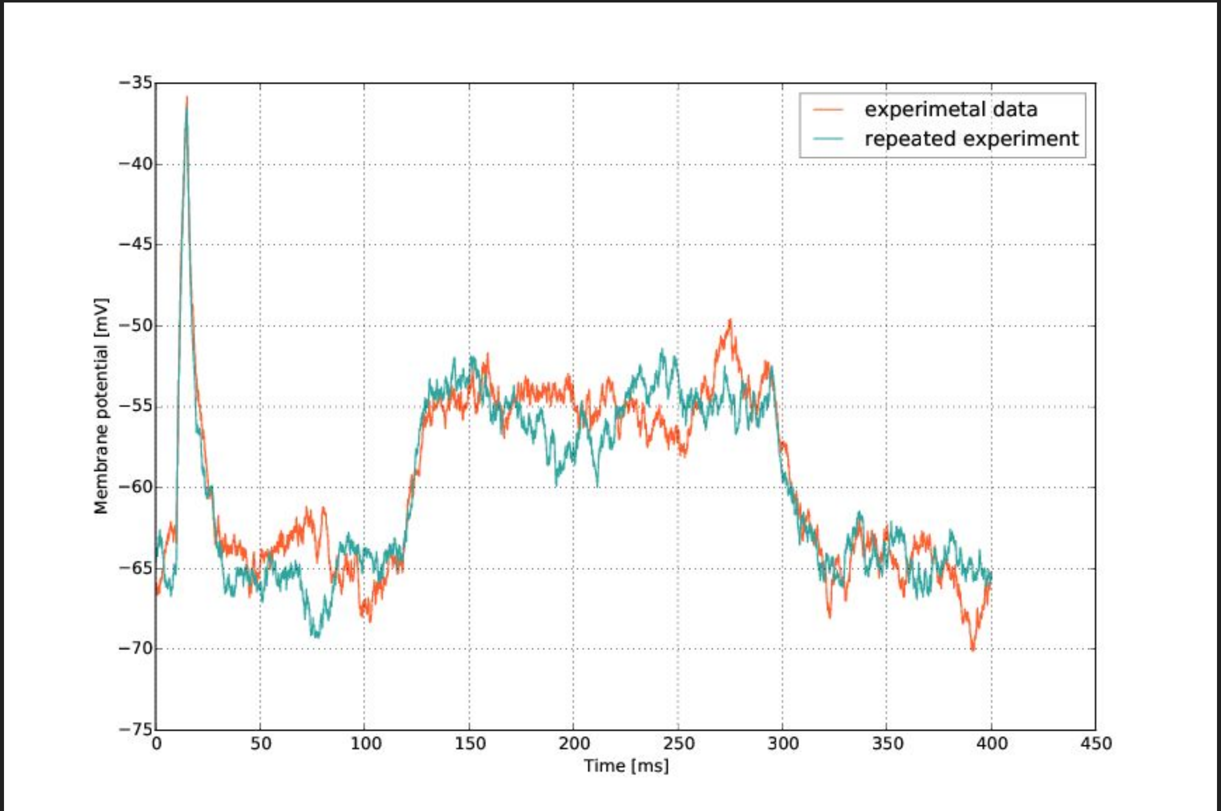
The main reason for the uncertainty is that the model is fitted to noisy data, so that a repeated measurement would result in different estimated parameters.

Finally, this method tells us nothing about how our estimates for these parameters may be interdependent.

Fitting model to noisy data – example



First experiment fit

Ra: 100 [Ohm cm]

cm: 1.01 [uF/cm^2]

gpas: 0.000102 [uS/cm^2]

Second experiment fit

Ra: 111 [Ohm cm]

cm: 1.2 [uF/cm^2]

gpas: 0.00011 [uS/cm^2]

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That is possible with the method of Bayesian inference.

How the method works

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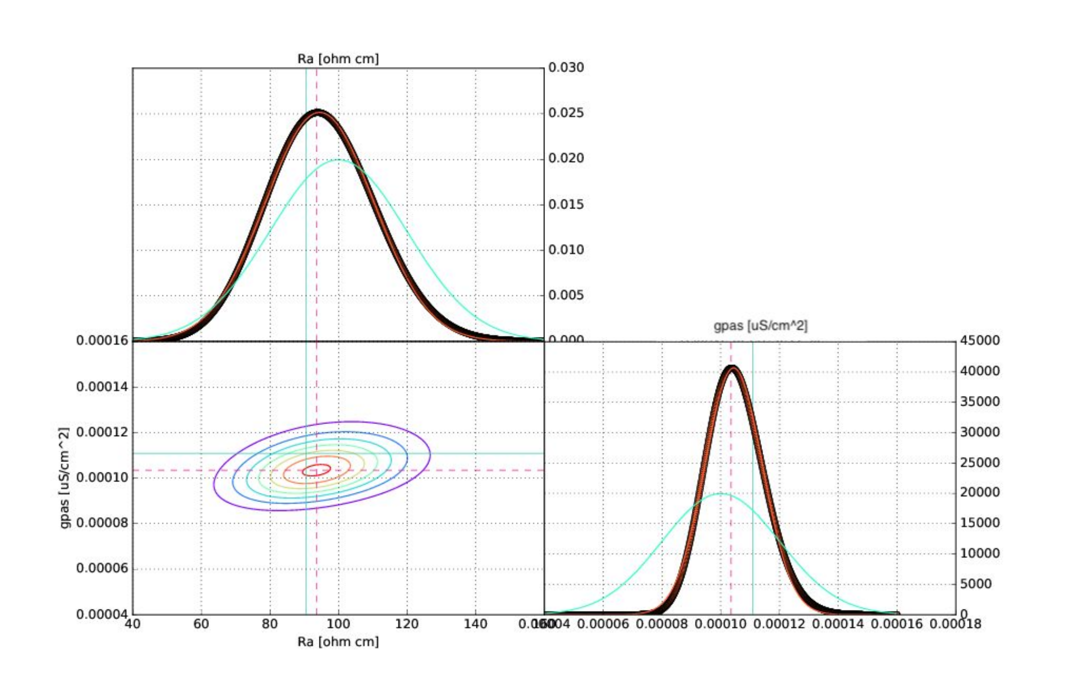
3. Finally we can compute the posterior probability distribution which combines our prior knowledge with the information gained from the experimental data (the likelihood).

Bayesian Inference

We have a probability distribution over the parameter space instead of a single best-fitting value



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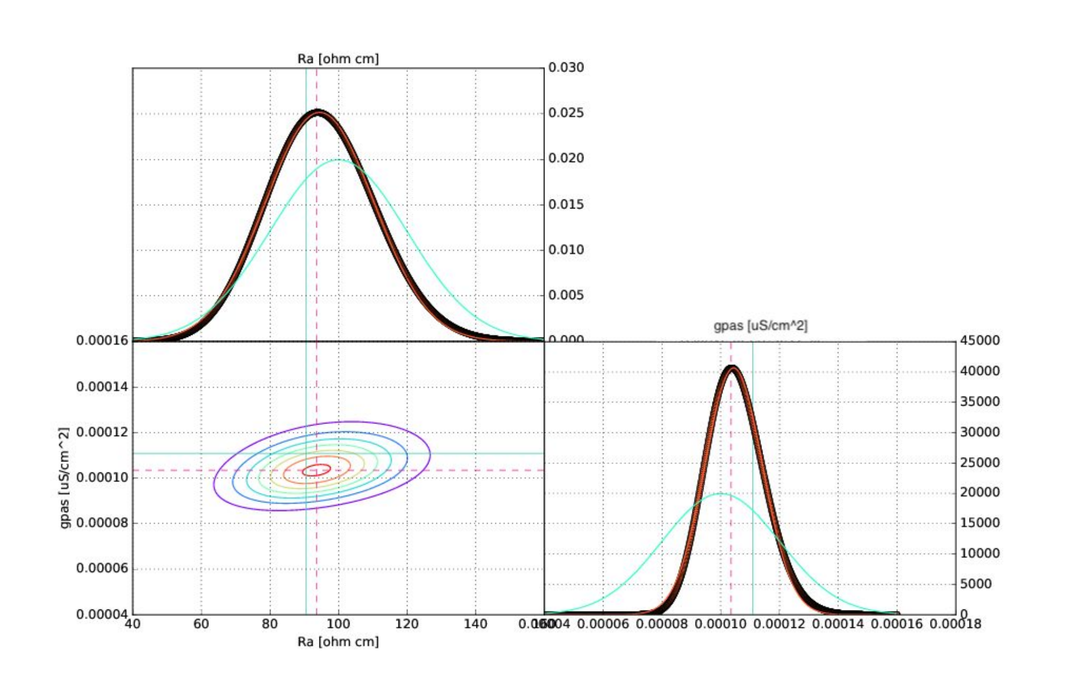

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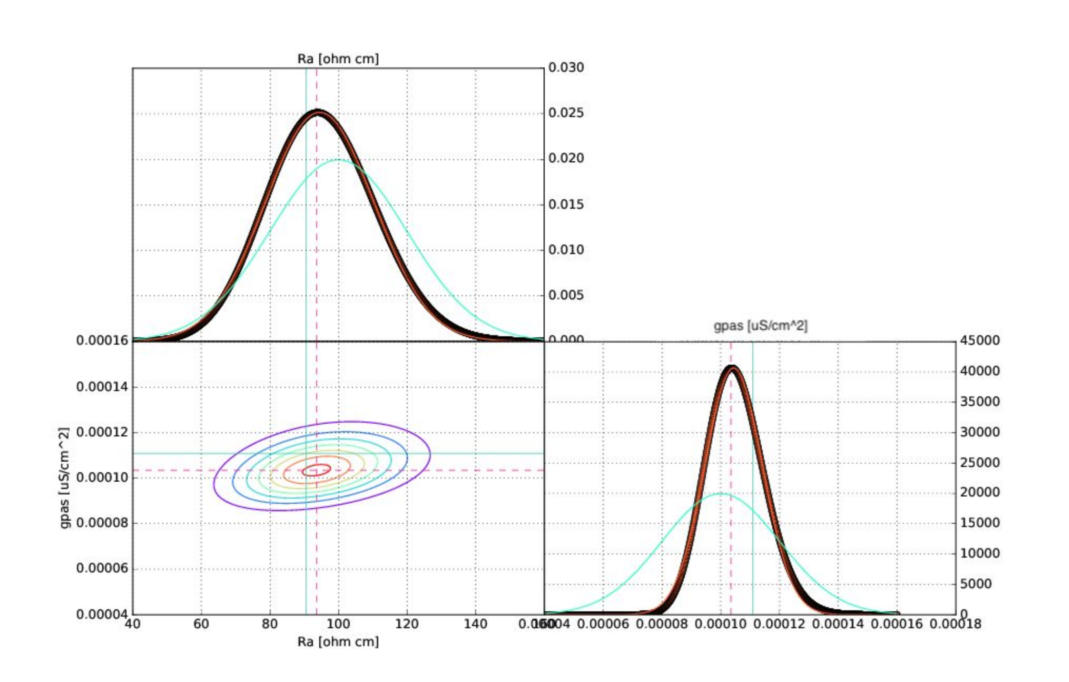

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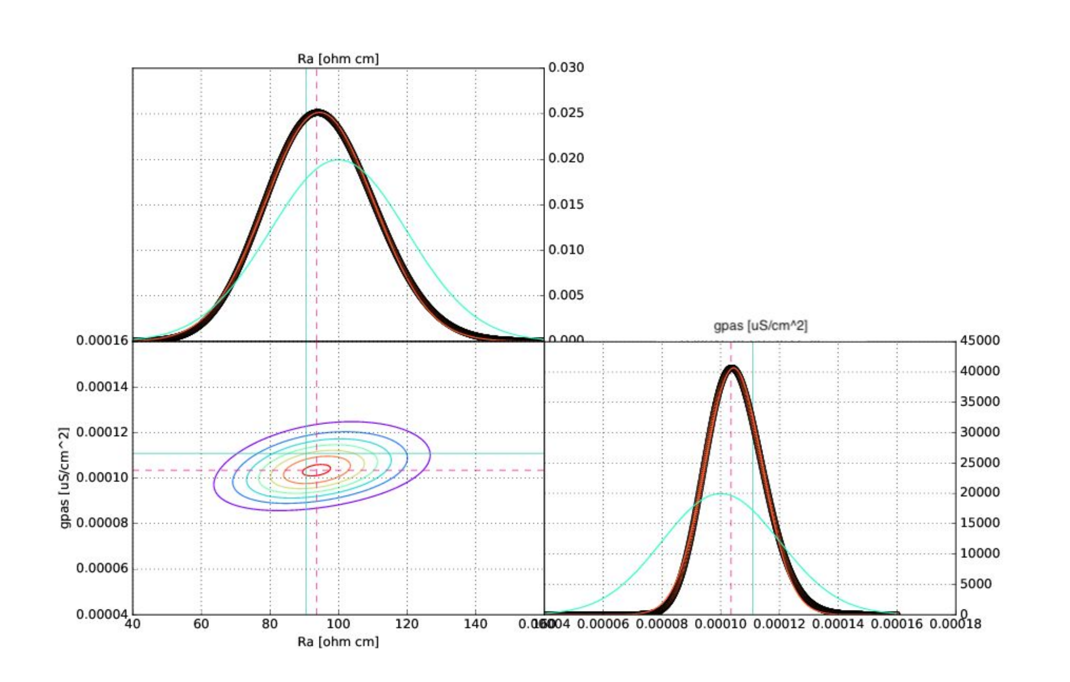
- The joint distributions illustrate the interconnections of the model parameters



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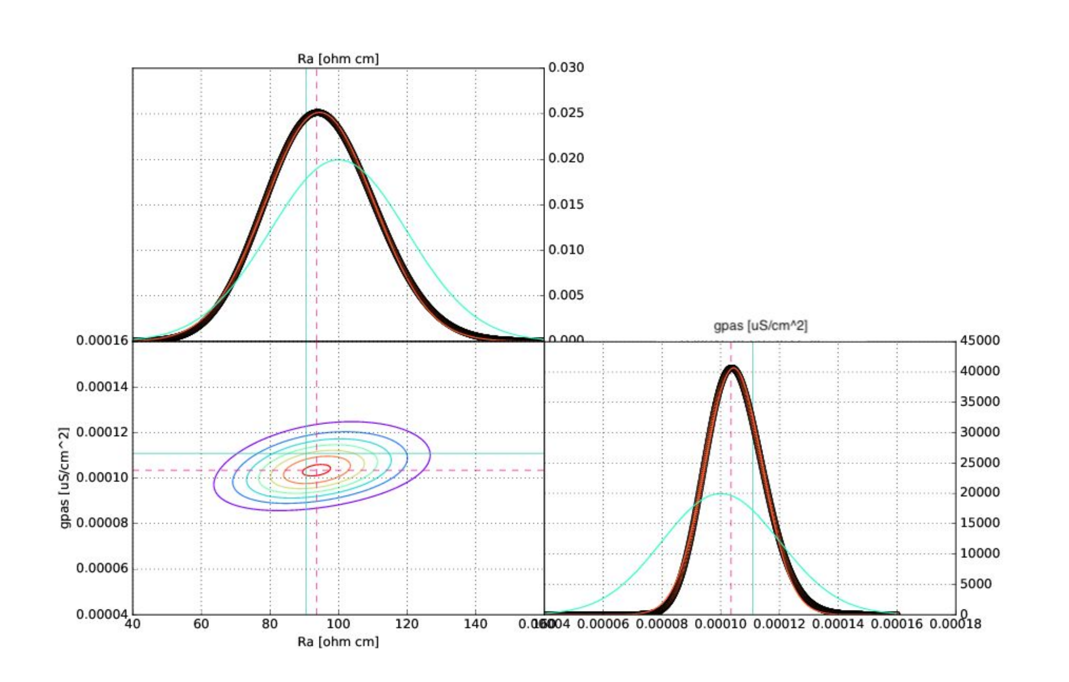

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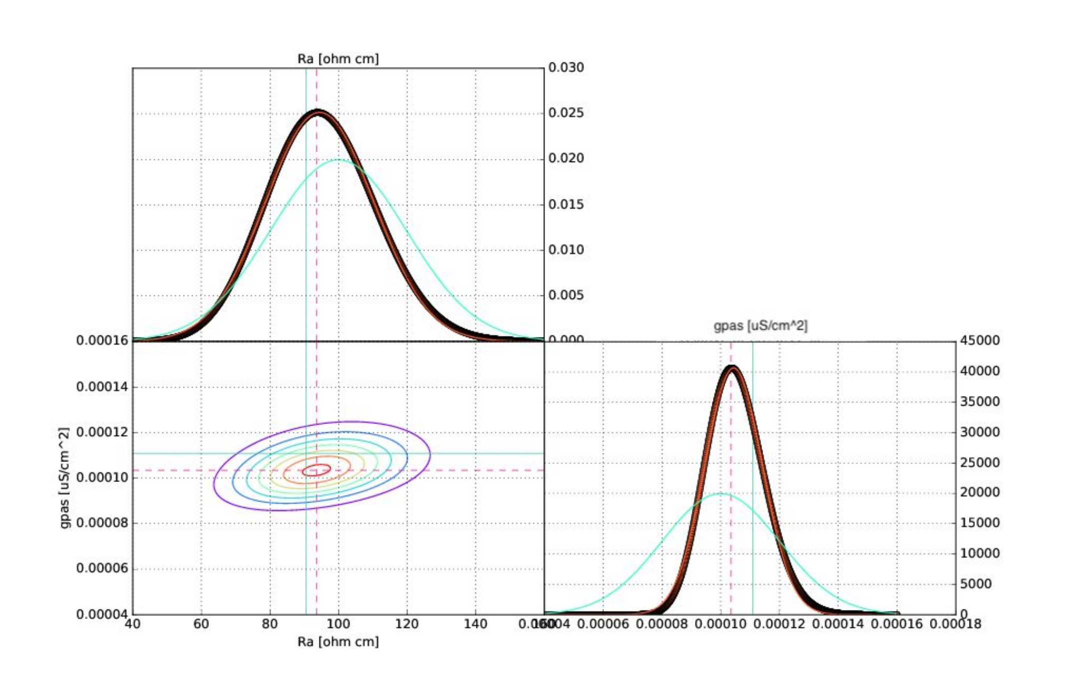
- The joint distributions illustrate the interconnections of the model parameters
- This method considers the experimental noise – no repeat is needed if the noise model is known.
- Finally we can compare experimental protocols and evaluate which one contains more information about the parameters

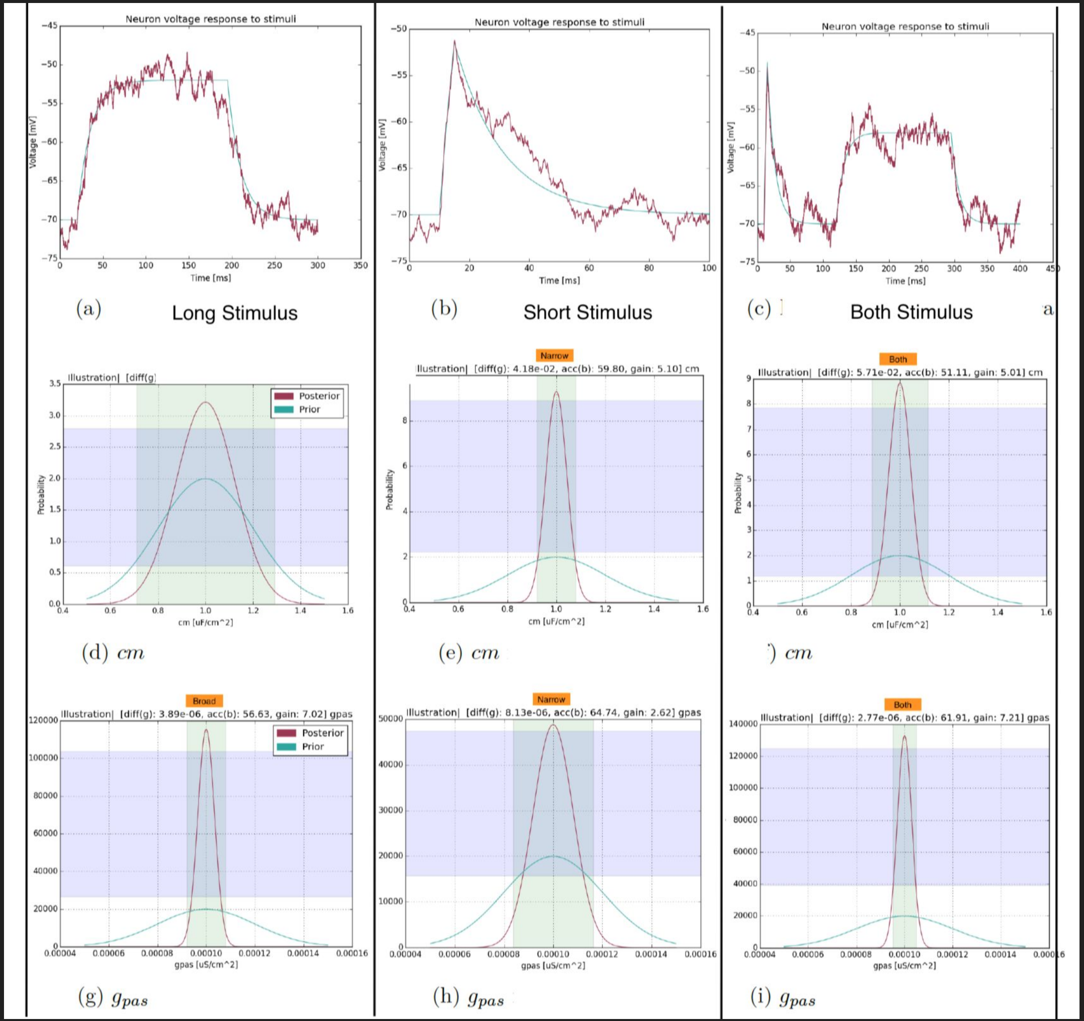


Compare protocols – example

Different parameters can be measured more accurately with different experimental protocols.

cm: transient part

gpas: constant part



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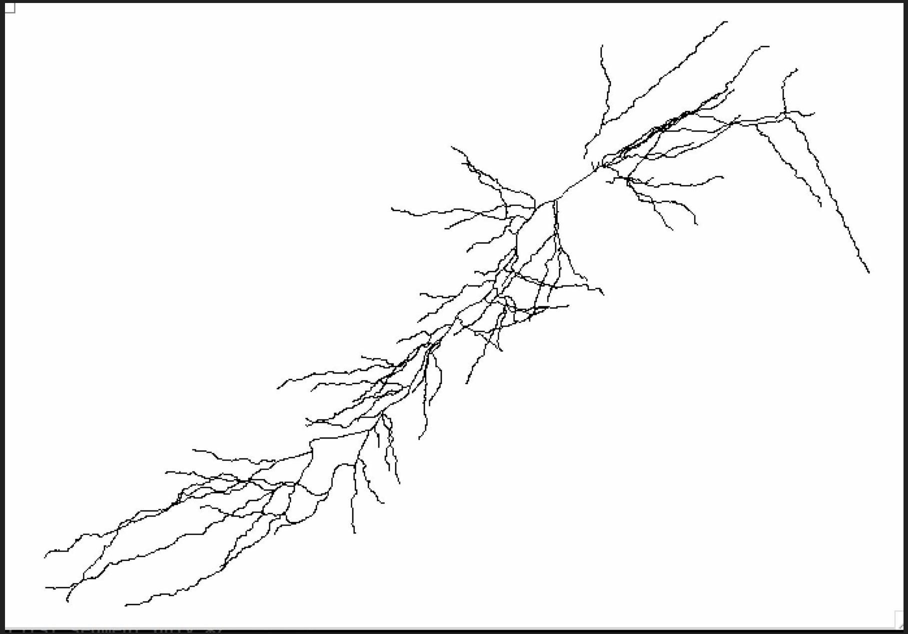
We can help to design experiments to maximize efficacy.

We only have to know the properties of the noise to be able to create synthetic data on which we can run simulations.

Application to real morphology

We executed our analysis on a real 3D reconstructed morphology model and estimated Ra and gpas parameters.



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We executed our analysis on a real 3D reconstructed morphology model and estimated Ra and gpas parameters.

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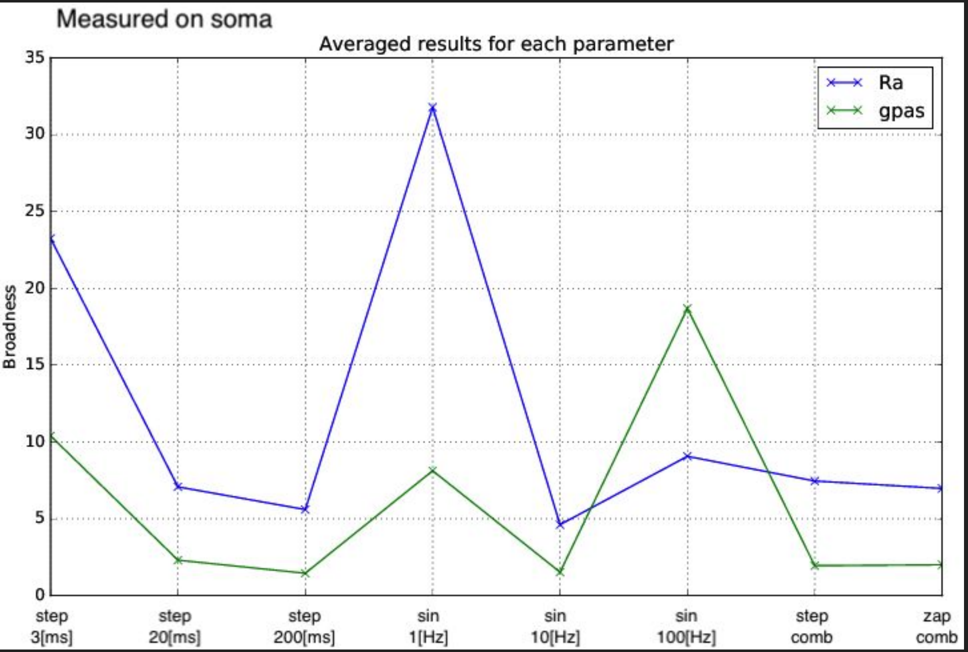
We used the broadness of the posterior probability distribution (compared to the prior distribution) to measure the information content of the experiment.

Comparing protocols



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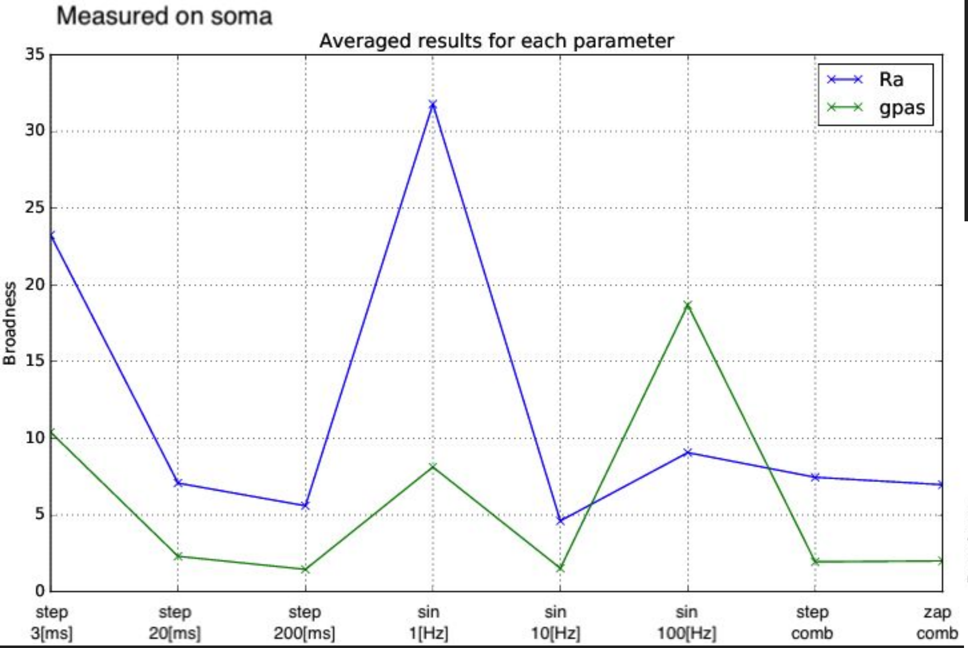
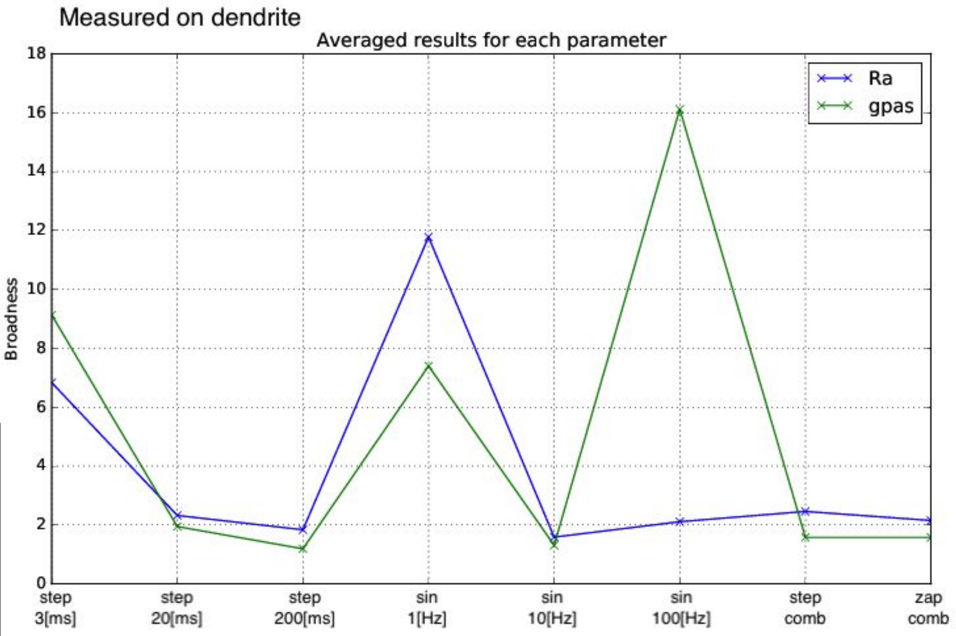


and when current was injected and membrane potential was recorded in the dendrite.



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Finally, this is a general procedure, which can be applied to other problems.

Acknowledgement

Szabolcs Káli

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Tamás F. Freund

Thank you for your attention!